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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/733,640
Filing Date: December 08, 2000
Appellant(s): MCHUGH ET AL.

Jonathan Taylor
Registration No. 48,338
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 20, 2006appealing from the Office action mailed June 9, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,525,646	LUNDGREN et al	6-1996
6,432,438	SHUKLA	8-2002

WO 88/07366	BATEMAN et al .	10-1988
6,130,200	BRODBECK et al	10-2000

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A) The rejection of claim 66 is under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

B) Claims 1, 5-7, 17-18, 34, 38, 51-53, 55-56, 58, 60, 66-67 are rejected under 35 U.S.C. 102(b) as being anticipated by US patent 5,525,646 to Lundgren et al. The rejection over claim 59 is withdrawn.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (instant solvent, acetyl tributyl citrate).

The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50. The polymer material is made by mixing the polymers and plasticizer to provide a homogenous **solution**. The solution is then allowed to solidify overnight.

Lundgren discloses implanting the polymer compositions into the periodontal defects of monkeys wherein the material is inserted into the oral cavity. See column 10, lines 34-45.

Note that the limitation of claim 58 must be inherent since the prior art and the instant claims recite the same structure with the same components unless the instant multilayer configuration is due to conditions that are not recited in the claims. If the latter is the case, then the applicant must include the conditions which provides the limitation.

With regard to claim 66, it is the examiner's position since the prior art teaches a polymer *solution*, it is capable of being dispensed from a 20-gauge needle.

C) Claims 1, 3, 5-7, 17-18, 34, 38, 49, 51-53, 55-56, and 58-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of US patent 5,525,646 to Lundgren et al.

Shukla teaches a biodegradable vehicle containing a drug, at least two plasticizers (solvent) selected from NMP, PEG, triacetin, etc, and at least one biodegradable polymer, which is injected into an organism. See abstract. The polymers may be selected from polyesters, polyorthoesters, polyanhydrides, polyaminoacids, pseudopolyamino acids, polyamides, polyalkylcyanoacrylates, and polyphosphazenes. A mixture of polymers may be used to tailor either the release characteristics of BAS in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both. See column 5, lines 55-67. The reference teaches the blending of two different biodegradable polymers with varying crystallinity

and amorphous states to tailor release characteristics of the delivery system. See column 4, lines 25-35.column 9, lines 30-35, and examples. The method of mixing the polymer, solvent, and drug are taught in examples. Note that NMP has a miscibility of a miscibility in water of 7% or less as defined by instant specification.

Although, Shukla teaches the blending of polymers according to their properties to manipulate release rate, Shukla et al do not exemplify the use of a polymer blend consisting of an amorphous polymer and crystalline polymer. Shukla exemplifies an amorphous polymer.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (solvent). The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50. Lundgren also discloses that a small amount of crystalline polymers to amorphous polymers drastically reduces swelling of the material. Lundgren discloses that swelling has a negative influence since it forces increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla et al and Lundgren and add a biodegradable crystalline polymer. One would have been motivated to do so since Lundgren teaches the criticality of having malleability and mechanical strength in an implant. Further, Lundgren teaches adding crystalline polymers to amorphous polymers reduce swelling of the implant, thus increasing mechanical strength of the implant. Therefore, one would have been motivated to add a crystalline polymer to Shukla's implant composition to provide mechanical strength to the implant once it is inserted in the body and reduce swelling of the material in the body.

Moreover, one would have been motivated to look to Lundgren's specific teaching that the instant polymer blend provides for an appropriate malleability and mechanical strength and apply it to Shukla's broad teaching of varying the properties, such as crystallinity and amorphous states, of the biodegradable polymers.

D) Claims 1, 3-18, 17-19, 34, 38, and 49-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,130,200 to Brodbeck et al in view of US patent 5,525,646 to Lundgren et al or vice-versa wherein the claims of 3-4, 8, 19, 49-50, 54, 57, 59, 61-65, 68-72 are rejected over Lundgren in view of Brodbeck.

Brodbeck et al disclose an injectable gel composition containing a biocompatible polymer(s), ethyl or benzyl benzoate, instant biocompatible component solvent , a bioactive agent, and an emulsifier for the active agent. See column 7, lines 25-35 and column 13, lines 50-65. (Note Examples, Tables 1-2) Brodbeck teaches biodegradable polymers include polylactides, polyglycolides, polyanhydrides, polydioxanones, polycaprolactone, PVP, etc. and mixtures thereof. See column 10, lines 65-68. Brodbeck teaches a solvent having a solubility in water of

less than 7% allows for suitable burst control and sustained release of the beneficial agent. The invention is directed to a method of systemically or locally administering a beneficial agent to a subject by implanting the gel into the subject. Lastly, Brodbeck teaches that rapid water intake into a polymer implant can result in an implant with pore structures causing a burst effect. See column 4, lines 24-40.

Although Brodbeck teaches mixtures of biodegradable polymers, does not specifically teach the instant polymer blend of an amorphous polymer with a crystalline polymer.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (solvent). The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50. Lundgren teaches the use of only the amorphous polymer causes water swelling which effects the stability and causes the implant to have pores, perforations, depressions, etc. See the entire discussion spanning 5-7. Lundgren discloses that a small amount of crystalline polymers to amorphous polymers drastically reduces swelling of the material. Lundgren discloses that swelling has a negative influence since it forces

increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Brodbeck et al and Lundgren and utilize a combination of an amorphous polymer and a crystalline polymer. One would have been motivated to do so since Lundgren teaches the criticality of having malleability and mechanical strength a biodegradable implant. Lundgren teaches that the use of an amorphous polymer provides malleability so that the implant can be formed to the desired shape and fit the implanting region but the sole use of an amorphous polymer causes instability of an implant by creating pores, perforations, etc. Thus, Lundgren teaches adding crystalline polymers to amorphous polymers to reduce swelling of the implant, thus increasing mechanical strength of the implant. Therefore, one would have been motivated to add a crystalline polymer to Brodbeck's implant composition to provide mechanical strength to the implant once it is inserted in the body and reduce swelling of the material in the body. Further, one would have reasonably expected success by combining the references since Brodbeck recognizes that polymer implants suffer from instability caused by swelling and provides a solution and although Brodbeck provides one solution to the problem, a skilled artisan would have been motivated to further prevent water uptake by adding a crystalline polymer.

Conversely, it would have been obvious to utilize the instant biocompatible solvent and emulsifying agent of Brodbeck's in Lundgren's formulation. One would have been motivated to utilize an emulsifying agent since Brodbeck teaches on column 6, lines 55-60 the use of an emulsifying agent to emulsify the active agent into the polymer. Further, one would have been

motivated to utilize the instant solvent and biocompatible solvent to further reduce the water intake of the implant and prevent an unwanted burst effect as taught by Brodbeck.

E) Claims 1, 3, 5, 34, 38, 49-49, 51, and 58-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of WO 88/07366 to Bateman et al.

Shukla teaches a biodegradable vehicle containing a drug, at least two plasticizers (solvent) selected from NMP (biocompatible solvent), PEG, triacetin (biocompatible component solvent), etc, and at least one biodegradable polymer, which is injected into an organism. See abstract. The composition is injected with a syringe, implanted, or it is applied directly to tissues of animals and humans. See column 3, lines 40-45. The composition is in the form of a viscous liquid, gel or paste. See column 4, lines 5-10. The polymers may be selected from polyesters, polyorthoesters, polyanhydrides, polyaminoacids, pseudopolyamino acids, polyamides, polyalkylcyanoacrylates, and polyphosphazenes. A mixture of polymers may be used to tailor either the release characteristics of BAS in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both. See column 5, lines 55-67. The reference teaches the blending of two different biodegradable polymers with varying crystallinity and amorphous states to tailor release characteristics of the delivery system. See column 4, lines 25-35, column 9, lines 30-35, and example 29. The method of mixing the polymer, solvent, and drug are taught in examples. Note that NMP has a miscibility in water of 7% or less as defined by instant specification. The vehicle is sterilized before packing. See column 3, lines 14-15.

Although, Shukla teaches the blending of polymers according to their properties to manipulate release rate, Shukla et al do not exemplify the use of a polymer blend specifically comprising an amorphous polymer and a crystalline polymer.

Bateman et al disclose a tablet composition containing a crystalline polymer and an amorphous polymer. See abstract. Bateman et al teach partially crystalline polymers provide for an immediate release whereas amorphous polymers provide for a prolonged release. See page 7, lines 25-35. Further, Bateman teaches that blending crystalline and amorphous polymers in various ratios, a range of active release can be provided. See page 8, lines 1-6.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla et al and Bateman et al and specifically utilize a polymer blend of an amorphous polymer and a crystalline polymer. One would have been motivated to do so since Bateman teaches that amorphous polymers tend to provide a sustained release whereas crystalline polymers provide a immediate release, and by varying the ratio of both types of polymer, the desired release rate can be obtained. Therefore, one would have been motivated to look to Bateman's specific teaching that the instant polymer blend provides for the desired release rate and apply it to Shukla's broad teaching that varying the properties, such as crystallinity and amorphous states of the biodegradable polymers tailors the release rate of the delivery device, to manipulate the release rate of Shukla's implant.

(10) Response to Argument

A) The rejection of claim 66 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn.

B) Claims 1, 5-7, 17-18, 34, 38, 51-53, 55-56, 58, 58, 60, 66-67 are rejected under 35 U.S.C. 102(b) as being anticipated by US patent 5,525,646 to Lundgren et al.

Appellant argues that the examiner has not given the term "injectable" patentable weight. Further, appellant argues that the examiner has not given the term "injectable" its proper meaning as defined in the specification. Appellant argues that an injectable composition for administration of a bioactive agent is described in the specification as a "fluid mixture'" that "transforms into a depot upon contact with the native fluid in the body'" when injected into a patient. Appellant argues this is in contrast to pre- formed surgical implants and tablets for oral delivery. Appellant argues that Lundgren discloses biodegradable compositions for use in tissue regeneration, where the composition is both malleable and dimensionally stable. Appellant acknowledges the reference describes a malleable composition as having a shape that "can be adapted to the shape of the region to be covered, often in a three-dimensional fashion." Appellant argues that administration of the compositions involves forming the composition into the desired shape and then surgically inserting the shaped composition into the patient. Thus, appellant argues there is no disclosure in Lundgren of an *injectable* composition.

Firstly, the examiner points out that the term "injectable" is given weight to the extent that the composition must be capable of being injected. Lundgren discloses a malleable composition comprising a 1) biodegradable crystallizable polymer; 2) a biodegradable amorphous polymer; 3) a biocompatible solvent having a miscibility with water less than 7% by weight; and 4) a bioactive agent. Moreover, the polymer composition exists in a solution state prior to solidification. Column 5, lines 50-60 discloses" "Approximately 25 g of polymer and plasticizer were dissolved in 250 ml of methylene chloride in order to obtain a homogeneous

solution. The solution was placed in a cupboard overnight in order to allow most of the solvent to evaporate in order to form a polymer film of the mixture." Thus, Lundgren's composition is *capable* of being injected since it exists in a solution state prior to solidification via evaporation.

With regard to the composition claims, the examiner notes that "injectable" in claim 1 occurs in the preamble. It is the examiner's position that the preamble merely recites the purpose of a process or the intended use of a structure and the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). The examiner further respectfully points out that the prior art is capable of performing the intended use, then it meets the claims. In instant case, Lundgren discloses a polymer composition comprising the same physical components and the composition exists in a solution form until solidified. Thus, Lundgren's polymer solution is capable of performing the intended use, i.e. being injected. Moreover, the instant invention and Lundgren will implicitly form a solid depot over time regardless of being solidified *in vivo* or *ex vivo*. The examiner notes that appellant has not argued that the compositions are different, appellant only argues the merits of the term "injectable". Therefore, the only difference between the prior art and the instant invention is that the prior art solidifies the composition *ex vivo* and appellant argues that the composition is solidified it *in vivo*. Hence, it is respectfully submitted that the instant composition as claimed is not patentably distinct from the composition disclosed by the prior art.

Appellant argues that the examiner has attempted to correlate the polymer solution, which is an intermediate product, to the instant injectable composition.

The examiner again points out that the instant invention also exists in a polymer solution before solidifying into a three-dimension depot. Thus, in essence the composition claimed by applicant is also an intermediate prior to solidification in the body.

The examiner points to the instant specification to substantiate this position.

Firstly, the examiner points to page 12, lines 8-15 wherein appellant discloses:

> The pharmaceutical compositions may be in the form of a sterile injectable aqueous or oleagenous suspension. This suspension may be formulated according to the known art using those suitable dispersing or wetting agents and suspending agents which have been mentioned above. The sterile injectable preparation **may also be a sterile injectable solution** or suspension in a non-toxic parenterally-acceptable diluent or solvent, for example as a solution in ethyl benzoate.

Secondly, the examiner points to page 17 of the instant specification which discloses:

> Since the implant systems of the present invention preferably are formed as viscous gels, the means of administration of the implants is not limited to injection, although that mode of delivery may often be preferred. Where the implant will be administered as a leave-behind product, it may be formed to fit into a body cavity existing after completion of surgery or it may be applied as a flowable gel by brushing or palleting the gel onto residual tissue, or bone. Such applications may permit loading of beneficial agent in the gel at concentrations above those typically present in injectable compositions. **It is also possible to form the depot outside the body and then to implant the depot surgically. In this case, the mixture can be formed, and then the solvent removed, for example by evaporation.**

Therefore, as evidenced by the specification the instant claims are also directed to an intermediate since the polymers also exists in a solution or flowable gel form prior to solidification *in vivo* or *ex vivo*.

The examiner further points out that Lundgren on column 5, lines 50-60 discloses the same method of making an ex vivo depot as disclosed by appellant on page 17 (cited above):

> "Approximately 25 g of polymer and plasticizer were dissolved in 250 ml of methylene chloride in order to obtain a homogeneous solution. The solution was placed in a

> cupboard overnight in order to allow most of the solvent to evaporate in order to form a polymer film of the mixture."

Thus, the composition of the prior art and the instant invention are the **same** regardless of whether the composition is solidified inside the body or outside the body. Moreover, it is clear from appellant's disclosure on page 17 that the composition's components do not change based on the method of solidification (*in vivo* versus *ex vivo).*

Appellant argues that the composition disclosed by Lundgren cannot be used as a control release device for bioactive agents.

The examiner points to column 5, lines 43-50 wherein Lundgren discloses:

> The material compositions include compositions that **are suitable as vehicles for the delivery of biochemical substances**, e.g. antibiotics such as tetra and minicycline, antiseptics such as clorhexidine, and growth stimulating substances such as Transforming Growth Factor beta, Insulin-like Growth Factor 1, Insulin-like Growth Factor 2, Platelet Derived Growth Factor and Bonemorphogenic Growth Protein.

With regard to the method of making claim 38, the examiner points out that the claim is directed to "A method of making an injectable composition for administering a bioactive agent comprising *combining the ingredients* wherein the ingredients comprise a biodegradable crystallizable polymer; a biodegradable amorphous polymer; a biocompatible solvent having a miscibility with water less than 7% by weight; and a bioactive agent". The claims do not specify that the composition is solidified after injecting it into the body, i.e. *in vivo*. Thus, the examiner respectfully points out that claim 38 is neither limited to making solidifying the composition in the body nor does the claim exclude solidification of the polymer composition *ex vivo*. Lundgren discloses on column 10, lines 34-45 that the polymer material is made by mixing the polymers and plasticizer to provide a homogenous **solution**. It is the examiner's position that this reads on applicant's limitation "combining the ingredients".

With regard to the method of administering claims 34, 49-57, 67-72, the claims are directed to "A method of administering a bioactive agent comprising **inserting an injectable composition** for controlled release of a bioactive agent into an organism, wherein the composition comprises a biodegradable crystallizable polymer; a biodegradable amorphous polymer; a biocompatible solvent having a miscibility with water less than 7% by weight; and a bioactive agent". Appellant argues that injectable limits the claim to an injection of a fluid mixture via a needle. Appellant argues that the definition of injectable composition is that it is a fluid mixture that is administered via a needle. The examiner respectfully points out that although appellant argues that injectable composition is defined in the specification, the specification does not clearly define the term inject**able**. The examiner points out that the specification defines only the term inject**ion** as a fluid mixture transforms into a depot upon contact with the native fluid in the body. However, injection and injectable are two different terms, which is consistent with appellant's use of the term in the specification and claims. The examiner offers the following as evidence to substantiate the difference between the two terms.

Firstly, the examiner cites page 3 of the instant specification which discloses:

> In another embodiment of the invention, there is provided a method of administering a bioactive agent, comprising inserting into an organism a mixture of biodegradable crystallizable polymer and biodegradable amorphous polymer. **The inserting may be by injecting.**

Secondly, the examiner cites page 16 of the specification which discloses:

> For an implant administered by injection, the fluid mixture transforms into a depot upon contact with the native fluid in the body. This depot is characterized by its phase separation from the physiological fluid and its decreased fluidity relative to the original mixture. The depot may be a semi- fluid gel, it may be a solid, or it may have an intermediate rigidity.

> Since the implant systems of the present invention preferably are formed as viscous gels, the means of administration of the implants is not limited to injection, although that mode of delivery may often be preferred. Where the implant will be administered as a leave-behind product, it may be formed to fit into a body cavity existing after completion of surgery or it may be applied as a flowable gel by brushing or palleting the gel onto residual tissue, or bone. Such applications may permit loading of beneficial agent in the gel at concentrations above those typically present in injectable compositions. It is also possible to form the depot outside the body and then to implant the depot surgically. In this case, the mixture can be formed, and then the solvent removed, for example by evaporation.

Thirdly, page 17 of the specification discloses:

> **Alternatively, the syringe may be used to form a composite depot ex vivo, and the depot may be surgically inserted into an the organism.**

Clearly, it is noted that the term "injectable used in the parent claim 34 is not limited to injecting the composition via a needle as argued by appellant as evidenced by the specification. Moreover, the examiner points to dependent claim 59 wherein appellant claims "wherein inserting is by injecting". If appellant's independent claim 34 is only limited to injection as argued, then dependent claim 59 requiring insertion by injection would not be necessary. Clearly appellant also views "injectable" and "injecting" differently. The examiner notes this difference between inserting an inject**able** composition and inserting by inject**ion** and thus has withdrawn the rejection over claim 59. Therefore, the examiner respectfully points out that independent claim 34 does not limit the claim to a method of administering via injection and the claim is only is directed to inserting a composition that is capable of being injected.

Appellant argues that the examiner has made an unreasonable interpretation of "injectable" but it is the examiner's position that this interpretation is consistent with appellant's specification as discussed above and without a clear definition in the specification of the term "injectable", the examiner may give the term its broadest and most reasonable interpretation.

Webster dictionary defines injectable as: 1a) to introduce into something forcefully b) to force a fluid into (as for medical purpose); 2 to introduce as an element or factor in or into some situation or subject. Thus, keeping this definition in mind, the examiner points out that Lundgren forms the polymer material to fit into the periodontal defects of the oral cavity. As acknowledged by appellant, Lundgren teaches the composition is described as malleable; i.e. without shape. Lundgren teaches malleability refers to a material that has little or no memory so that the material can be adapted to the shape of the region to be covered. See column 1, lines 32-44. This is consistent with the appellant's disclosure on page 16 which discloses, "Where the implant will be administered as a leave-behind product, it may be formed to fit into a body cavity existing after completion of surgery or it may be applied as a flowable gel by brushing or palleting the gel onto residual tissue, or bone. It is also possible to form the depot outside the body and then to implant the depot surgically." The examiner again respectfully stresses that appellant does not limit independent claim 34 to "injecting" but rather recites "injectable".

Appellant argues that injectable composition is limited to a viscosity of 18-20 gauge needle as defined by the specification. The examiner again respectfully points out that the specification does not clearly define injectable and does not define the composition to a certain viscosity. The examiner points to page 16 of the specification:

> "A consideration for administration by injection is the viscosity of the mixture. It is preferred that the viscosity is such that the mixture can be made to flow easily thorough an 18-20 gauge needle". See page 16, lines 17-20.

Thus, it can be seen that the specification does not clearly limit the composition to a specified viscosity and rather teaches a preferred embodiment.

C) Claims 1, 3, 5-7, 17-18, 34, 38, 49, 51-53, 55-56, and 58-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of US patent 5,525,646 to Lundgren et al.

Appellant argues that Lundgren teaches away from the injectable composition and Shukla et al teach an injectable composition. Appellant argues that Lundgren teaches away from Shukla et al. Thus, appellant argues that it is improper to combine the references.

Appellant's arguments pertaining to Lundgren teaching away from injecting the composition is unsubstantiated. Appellant merely argues this point without specifying the column in which Lundgren purportedly teaches away from an injectable composition. It appears appellant is assuming that since Lundgren exemplifies solidification of the polymer solution *ex vivo*, i.e. prior to implanting in an organism, this constitutes a teaching away. Further, it appears appellant assumes that a composition that is dimensionally stable is equivalent to a teaching that it cannot be injectable. Firstly, the examiner points out that Shukla's implant and the instant invention also implicitly form a solid depot after implantation. The stability of the implant after solidification does not mean it cannot be injectable. As discussed above, it is the examiner's position that Lundgren's composition is capable of being injected and thus reads on the term "injectable". Lundgren discloses composition comprising the instant 1) biodegradable crystallizable polymer; 2) a biodegradable amorphous polymer; 3) a biocompatible solvent having a miscibility with water less than 7% by weight; and 4) a bioactive agent. Moreover, the polymer composition exists in a solution state prior to solidification. Thus, Lundgren's composition is *capable* of being injected since it exists in a liquid state prior to solidification via evaporation. The examiner relies on the secondary reference, Lundgren, to cure the deficiencies

of the polymer composition in the primary reference, Shukla. The fact solidification *prior* to implantation versus solidification *after* implantation does not change the examiner's motivation to combine the references since it does not affect the physical components of the composition.

Shukla teaches at least one biodegradable crystallizable polymer, a biocompatible solvent having a miscibility with water less than 7% by weight; and 4) a bioactive agent. Shukla utilizes amorphous polymers in the examples. Thus, the only deficiency in Shukla is the exemplification of a crystallizable polymer and an amorphous polymer. However, Shukla generally teaches mixing a blend of polymers to tailor either the release characteristics of biologically active substance (BAS) in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both on column 5, lines 55-67. Shukla further teaches the blending of two or more different biodegradable polymers with varying crystallinity and amorphous states to tailor release characteristics of the delivery system and rheology of the vehicle on column 4, lines 25-35. Lastly, Shukla teaches using blends of polymers with different crystallinity can result in a biodegradable vehicle with varying degradation rates whereas a amorphous polymer may degrade at a much faster rate that the rest of the polymers in the blend. See column 7, lines 40-45, and example 29. Therefore, although Shukla itself suggests the use of a crystalline polymer with an amorphous to tailor the release rate, the examiner relies on a secondary reference to provide further motivation for a skilled artisan to specifically utilize a mixture of an amorphous polymer and a crystalline polymer. Lundgren teaches the use of an amorphous polymer to provide malleability to the implant so that it can be adapted to the desired shape and further teaches adding a small amount of crystalline polymers to the amorphous polymers to drastically reduce swelling of the material. Lundgren discloses that swelling has a

negative influence since it forces increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55. Therefore, as stated in the rejection the motivation to add a crystalline polymer is to increase the mechanical strength of the implant. It is noted that appellant does not address the examiner's motivation and rather attacks the references individually and the term "injectable".

The examiner notes the following similarities between Shukla and Lundgren which provides a skilled artisan a reasonable expectation of success by the combination. Shukla teaches the vehicle may be injected, implanted, or applied directly to the site. See column 3, lines 40-45. The term "implant" encompasses depots that are made ex vivo and then implanted. Further examiner points out that Shukla's forms a solid depot after injecting the composition. Thus, the end product of both references is that it forms a solid depot. Secondly, the examiner points to Shukla's examples that demonstrate that the polymer composition is in a form of a liquid, gel, or paste prior to injection and the examiner points out that Lundgren's composition also exists in a liquid state prior to solidification. Lastly, both Shukla and Lundgren teach using the devices to deliver active agents. Thus, a skilled artisan would reasonably expect similar results in combining Shukla and Lundgren since both teach similar polymer composition that are capable of being injected and forms solid depots for controlled release of an active agent.

D) Claims 1, 3-18, 17-19, 34, 38, and 49-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,130,200 to Brodbeck et al in view of US patent 5,525,646 to Lundgren et al or vice-versa wherein the claims of 3-4, 8, 19, 49-50, 54, 57, 59, 61-65, 68-72 are rejected over Lundgren in view of Brodbeck.

Appellant argues that Lundgren teaches away from the injectable composition and Brodbeck et al teaches an injectable composition. Appellant argues that Lundgren teaches away from Brodbeck et al. Thus, appellant argues that it is improper to combine the references.

Appellant's arguments pertaining to Lundgren teaching away from injecting the composition is unsubstantiated. Appellant merely argues this point without specifying the column in which Lundgren purportedly teaches away from an injectable composition. It appears appellant is assuming that since Lundgren exemplifies solidification of the polymer solution *ex vivo*, i.e. prior to implanting in an organism, this constitutes a teaching away. Further, it appears appellant assumes that a composition that is dimensionally stable is equivalent to a teaching that it cannot be injectable. Firstly, the examiner points out that Shukla's implant and the instant invention also implicitly form a solid depot after implantation. The stability of the implant after solidification does not mean it cannot be injectable. As discussed above, it is the examiner's position that Lundgren's composition is capable of being injected and thus reads on the term "injectable". Lundgren discloses composition comprising the instant 1) biodegradable crystallizable polymer; 2) a biodegradable amorphous polymer; 3) a biocompatible solvent having a miscibility with water less than 7% by weight; and 4) a bioactive agent. Moreover, the polymer composition exists in a solution state prior to solidification. Thus, Lundgren's composition is *capable* of being injected since it exists in a liquid state prior to solidification via evaporation. The examiner relies on the secondary reference, Lundgren, to cure the deficiencies of the polymer composition in the primary reference, Brodbeck. The fact solidification *prior* to implantation versus solidification *after* implantation does not change the examiner's motivation to combine the references since it does not affect the physical components of the composition.

Brodbeck teaches at least one biodegradable polymer; a biocompatible solvent having a miscibility with water less than 7% by weight; an emulsifying agent and a bioactive agent. Brodbeck generally teaches the implant may have a blend of polymers. Thus, the only deficiency in Brodbeck is the specific teaching of a combination of a crystallizable polymer and an amorphous polymer. Lundgren teaches the use of an amorphous polymer to provide malleability to the implant so that it can be adapted to the desired shape. However, Lundgren teaches the use of only the amorphous polymer causes water swelling which effects the stability and causes the implant to have pores, perforations, depressions, etc. See the entire discussion spanning 5-7 and especially column 7, lines 45-55. Lundgren teaches adding a small amount of crystalline polymers to the amorphous polymers drastically reduce swelling of the material. Lundgren discloses that swelling has a negative influence since it forces increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55. Brodbeck on column 4, lines 24-40 recognizes that rapid water intake into a polymer implant can result in an implant with pore structures causing a burst effect. Therefore, as stated in the rejection the motivation to add a crystalline polymer is to increase the mechanical strength of the implant. A skilled artisan would have reasonably expected success from the combination since both Brodbeck and Lundgren both recognize the detrimental effect of rapid water intake and Lundgren provides one solution to reduce the swelling.

E) Claims 1, 3, 5, 34, 38, 49-49, 51, and 58-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of WO 88/07366 to Bateman et al.

Appellant argues that Shukla teaches injectable composition whereas Bateman teaches solid tablet formulations and thus the combination is improper. Appellant argues that one would

not expect success in the combination of the teaching of Shukla and Bateman and thus the combination Lastly, appellant argues that an attempt to incorporate the tablet formulation of Bateman into Shukla is improper since it would render the primary reference inoperable.

The examiner acknowledges that Bateman is directed to a controlled release tablet formulation and Shukla directed to a controlled release viscous gel, liquid, or paste. However, the examiner respectfully points out that "The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. " See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In instant case, the premise of the rejection is not to incorporate Bateman's tablet into Shukla. The examiner relies on Bateman to demonstrate the state of the art wherein it is known to blend polymers with different crystallinity to manipulate the release rate. Shukla generally teaches mixing a blend of polymers to tailor either the release characteristics of biologically active substance (BAS) in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both. See column 5, lines 55-67. Shukla teaches the blending of two or more different biodegradable polymers with varying crystallinity to tailor release characteristics of the delivery system. See column 4, lines 25-35. Moreover, Shukla teaches using blends of polymers with different crystallinity and hydrophobicity can result in a biodegradable vehicle with varying degradation rates. See column 7, lines 40-45, and example 29. Although, it is the examiner's position that Shukla itself suggests the use of a crystalline polymer with an amorphous to tailor the release rate, the examiner relies on Bateman to further

provide motivation to a skilled artisan to specifically utilize the polymer blend suggested by Shukla. Bateman clearly states on page 8 that "blending crystalline and amorphous polymer in various ratios, the tablets having a range of active ingredients release characteristics can be provided." Although, Bateman is directed to tablet formulations, Bateman demonstrates the general knowledge in the pharmaceutical art. The fact that the vehicle for an active agent is an implantable depot versus a tablet is irrelevant since the properties of the polymers do not change. Moreover, one would have expected Bateman's teachings to apply to Shukla since Shukla does in fact suggest that polymer blends with varying crystallinity change the release rate of the active. Clearly both references teach the same function of the crystalline polymer and amorphous polymers regardless of the mode of administering the composition and intended use of the composition.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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